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Hot News

New insights into the genetics of same-sex behavior

Across human societies, a fraction of men and women (around 2-10%) report engaging in sex with same-sex partners, either exclusively or, more frequently, in addition to having heterosexual partners (bisexuals) *(ACSF. Nature 1992; Melbye et al. Am J Epidemiol 1992; Bailey et al. Psychol Sci Public Interest 2016; Semenyna et al. J Sex Res 2017)* (Fig. 1). Another smaller subset of individuals report gender dysphoria (transgender), where sexual self-perception conflicts with the biological sex *(Hruz P. Linacre Q 2020)*.

Same-sex behavior runs more frequently in some families and is concordant more often in genetically identical twin pairs than in non-identical twin pairs or siblings, which could suggest a genetic influence on the trait. Moreover, homosexual behavior is also widespread in the animal kingdom.

A gay gene?

The search for genetic determinants of same-sex behavior has been examined multiple times without much support. During the past couple of years, two large studies have provided new robust insights.

The first study was conducted using 477,522 genetic sequences from individuals in the US and the UK *(Ganna et al. Science 2019)*. A genome-wide association study yielded five variants that stood out as being significantly associated with having same-sex behavior, though the effect was small—<1% when combined together. The autosomal loci linked to same-sex behavior were all associated to biological pathways that involve sex hormone regulation and olfaction. The analysis also surfaced more common variants that contribute between 8% to 25% of the variance in a population's sexual behavior. However, the conclusion was clear: a single gay gene did not exist. More likely there were thousands, many not yet discovered, and that environment was always going to play the most important role. In this regard, epigenetic changes might mediate the influence of environmental forces on the individual's biological substrate *(Ngun et al. Adv Genet 2014)*.

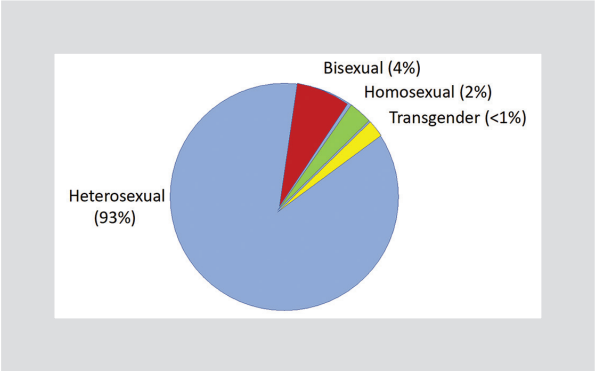

Figure 1. *Prevalence of sexual behavior in humans.*

In a last step, the authors tried to use the genetic markers they had found to predict the sexual behavior in an unrelated data set of 15,000 adults. They found almost no correlation, meaning that the individual-level prediction is null at this time. In other words, we cannot produce a polygenic risk score for the prediction of homosexuality.

Another intriguing finding in Ganna's study was that the genetic traits associated with same-sex encounters partially overlap with genes linked to mental health conditions, including depression and schizophrenia. This result is in agreement with prior studies that have shown a higher rate of mental disorders in LGTB persons (*Semlyen et al. BMC Psychiatry 2016*). The etiopathogenic mechanism for this association has remained uncertain until now.

Genetic traits for openness to experience

Same-sex sexual relationships occur in the animal kingdom across multiple species. Researchers have interpreted this behavior as a way of social acceptance and promotion, manifestation of closer friendship with someone, mechanism for improving self-knowledge, and/or preliminary training for successful mating with heterosexual partners *(Barron et al. Front Psychol 2020; 10: 2955; Luoto S. Arch Sex Behav 2020; 49: 2239-44)*.

To evolutionary biologists, the genetics of homosexuality seems counter-intuitive, a Darwinian paradox. Homosexual individuals will unlikely produce many

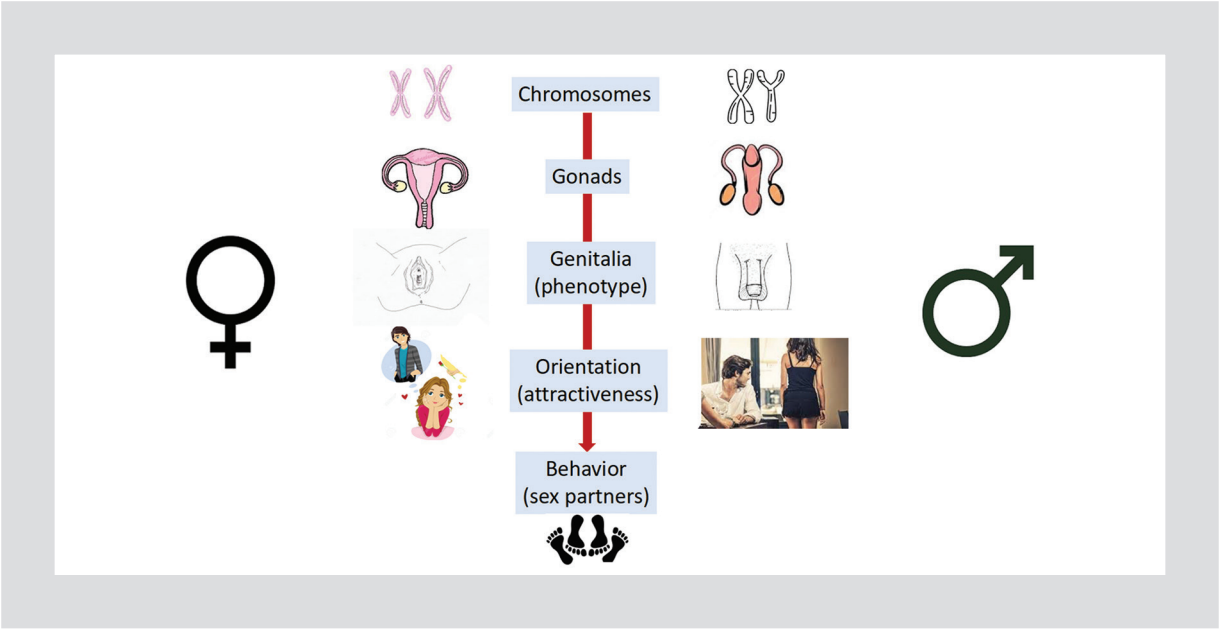

Figure 2. *Biological development of human sexuality.*

biological children. Thus, the genetic trait will rarely be passed on to future generations. If so, genetic variations associated with same-sex behavior would have eventually disappeared, unless it somehow helped people to survive or reproduce.

The second recent large study *(Zietsch et al. Nat Hum Behav 2021)* examined the number of sex partners in 358,426 heterosexual individuals from the UK and the USA. The authors found that many of the genetic traits associated with homosexuality were also linked to an increased number of partners in heterosexuals. In view of these results, they proposed that the identified genetic patterns that could be associated with homosexual behavior might also help heterosexual people to find heterosexual mates and reproduce. This phenomenon could explain why genes that predispose people to homosexuality continue to be passed down generations.

There are several caveats before accepting this hypothesis. First, the existence of birth control and fertility treatments negates many of the reproductive advantages that these genes might provide. Second, people might engage with more sexual partners now that many sexually transmitted diseases can be cured. Overall, people's behavior when it comes to sex and reproduction is highly culturally informed, and maybe digging into genetics is next to impossible.

An intriguing finding of the study was that people who had same-sex encounters shared genetic markers with people who described themselves as risk-taking and open to new experiences. Overall, the same genetic variants partly overlapped with those on a variety of other behavioral traits, including externalizing attitudes "*such as smoking, cannabis use, risk-taking, and the personality trait openness to experience*." In addition, analyses suggested that sexual behavior, attraction, identity, and fantasies are influenced by a similar set of genetic variants.

Sex biology

Sexual behavior has a biological substrate. The newly created zygote after fusion of the two parental gametes, the spermatozoid and the egg, carries either XX or XY chromosomes. All the descendant cells from this unique zygote show the same sexual load and determine a wide range of differences in gene expression in all newly differentiated cell tissues (Oliva et al. Science 2020). In the embryo, the *SRY* gene exclusively present in chromosome Y determines the development of masculine gonads (testicles), prostate, and the penis. Otherwise, the zygote differentiates as female, with ovaries, uterus, and vagina. After the first 2 months of intrauterine life, the male fetus continues to develop other masculine sexual traits, including neurological network platforms that characterize male brains in opposition to female brains *(Ingalhalikar et al. PNAS 2014).* After birth, secondary sexual traits steadily appear until complete sex-

ual maturity and fertility are achieved after puberty. Since then, and dictated by individual human choices, sexual behavior tends to follow sexual attraction (Fig. 2).

Based on biology, it seems that the environment (cultural, society, family, life style, etc.) must play the most important role for gay behavior. In other words, all scientific evidence supports that homosexuality should be more often considered "acquired" than "primed," and primarily determined by "nurture" rather than "nature."

Sex behavior in persons with congenital intersexual states or syndromes (i.e, congenital adrenal hyperplasia, Turner, Klinefelter, etc.) merit a separate discussion. The topic has nicely been reviewed recently *(Delot et al. Nat Rev Genet 2021)*.

Pushing up sex research

From the medical standpoint, investigations to find the determinants and mechanisms of medical conditions have been pushed for almost all kind of entities causing physical/mental disadvantages or linked to increased harm, such as obesity.

A recent viewpoint has highlighted that many LGTB people experience depression, substance use, HIV infection, violence, homelessness, etc. *(Sepulveda et al. JAMA Ped 2021)*. Therefore, inclusive efforts for this population must be encouraged, to avoid discrimination. However, attempts for normalization should not mean to oversight the problem. The lack of recognition of this condition may discourage medical research that ultimately might help affected persons *(Hruz et al. Linacre Q 2020)*. Even more, criticism and lack of support for rigorous sex research will cause tremendous damage diverting from finding any potential benefit, as recently highlighted in an editorial by JM Bailey entitled "How to ruin sex research" *(Arch Sex Behav 2019)*. As in the parody of the naked king, written by Hans Christian Andersen (1805-1875), silencing a problem may be more disastrous than confronting it.

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